Eur J Vasc Endovasc Surg 33, 742–746 (2007)
doi:10.1016/j.ejvs.2006.11.039, available online at http://www.sciencedirect.com on ScienceDirect

The Predictive Value of Haemodynamic Assessment in Chronic Venous Leg Ulceration

M.S. Gohel,[1] J.R. Barwell,[1] B.P. Heather,[2] J.J. Earnshaw,[2] D.C. Mitchell,[3] M.R. Whyman[1] and K.R. Poskitt[1*]

[1]*Cheltenham General Hospital, UK,* [2]*Gloucestershire Royal Hospital, UK, and* [3]*Southmead Hospital, UK*

Objectives. *The aim of this study was to assess the value of PPG in predicting healing and recurrence in patients with chronic venous ulceration.*
Methods. *500 patients with open or recently healed venous ulceration were treated with either multilayer compression or compression plus superficial venous surgery and followed up in specialist clinics as part of a clinical study. At initial assessment, VRT was measured using PPG with and without a below-knee tourniquet inflated to 80 mmHg to occlude superficial veins. Legs were stratified into groups with VRT <11 s, 11–20 s and >20 s and comparison of healing and recurrence rates between these groups was performed.*
Results. *VRT measurements were not achieved in 117 patients, primarily due to ankle stiffness. Of the remaining 383 patients, VRT without tourniquet did not correlate with ulcer healing ($p = 0.26$, 0.40) or recurrence ($p = 0.20$, 0.79, Log rank test) for legs treated with compression or compression plus surgery respectively. However, VRT readings taken with a below-knee tourniquet were predictive of ulcer healing ($p < 0.01$) and recurrence ($p = 0.05$, Log-rank test). The correlation was greatest for healing in legs treated with compression alone, where 24 week healing rates were 62%, 73% and 92% for legs with VRTs with tourniquet <11 s, 11–20 s and >20 s respectively ($p < 0.01$, Log rank test). For legs treated with surgery, 1 year recurrence rates were 24%, 10% and 3% for groups with VRTs with tourniquet <11 s, 11–20 s and >20 s respectively ($p = 0.03$, Log rank test).*
Conclusions. *Digital PPG assessment may predict ulcer healing and recurrence, but only by using a below-knee tourniquet. This information could aid the selection of patients with venous ulceration most likely to benefit from superficial venous surgery.*

Keywords: Photoplethysmography; Chronic venous ulceration; Haemodynamic assessment; Venous refill time; Superficial venous surgery.

Introduction

Chronic venous leg ulceration is an important cause of patient morbidity and health service expense[1] with an estimated prevalence of 1–2%.[2,3] In patients with a leg ulcer, colour venous duplex assessment can accurately identify anatomic patterns of venous reflux, potentially amenable to surgical correction.[4,5] Venous refill time (VRT) reflects the time taken for a limb to return to its resting venous pressure following calf muscle pump contraction. Long VRTs demonstrate normal venous function, whereas very short VRTs may indicate a greater severity of venous disease. This hemodynamic assessment may measure physiological venous disease and can be assessed using a variety of techniques. Digital photoplethysmography (PPG) is a minimally invasive procedure for the measurement of VRT that can be used with, or without an inflated below-knee tourniquet to compress superficial veins and mimic saphenous surgery.[6] This has been validated against more invasive techniques.[7]

Accurate assessment of the severity of venous dysfunction could help predict clinical outcomes. Although colour duplex provides important anatomic information about patterns of venous reflux, there is often a poor correlation between venous incompetence and clinical outcomes in the ulcerated leg.[8] VRT assessment is thought to reflect the severity of physiological venous dysfunction more accurately. It may also correlate with clinical outcomes, although this remains unproven. The aim of this study was to assess the value of VRT assessment using PPG in predicting healing and recurrence in patients with chronic venous leg ulceration.

*Corresponding author. Mr K.R. Poskitt, MD, FRCS, Department of Vascular Surgery, Cheltenham General Hospital, Sandford Road, Cheltenham GL53 7AN, UK.
E-mail address: keith.poskitt@glos.nhs.uk

1078–5884/000742 + 05 $32.00/0

Methods

All patients included in this study were part of the ESCHAR venous ulcer study.[9] Legs with CEAP grades C5 or C6 (open or recently healed ulceration) and superficial venous reflux were randomised to multilayer compression bandaging alone or compression plus superficial venous surgery. Patients were reviewed in specialist nurse-led leg ulcer clinics and VRT assessments were attempted in all patients at initial assessment using PPG.

Treatments

Legs with open ulceration were treated with weekly multilayer compression bandaging (Profore, Smith & Nephew, Hull UK) followed by class II elastic stockings (Duomed, Medi, UK) once healed. Those randomised to the surgery arm were offered additional saphenofemoral and/or saphenopopliteal junction disconnection with stripping of the great saphenous vein in the thigh and calf varicosity avulsions. All patients were investigated using colour venous duplex to assess superficial and deep venous segments. Patients unfit for general anaesthetic were treated with local anaesthetic saphenofemoral and/or saphenopopliteal junction disconnection alone. Procedures were guided by colour duplex findings and offered within 6 weeks of randomisation. Participants were followed-up monthly until ulcer healing, defined as complete re-epithelialisation of the wound. Patients with healed legs were invited for assessment 3-monthly up to 1 year. All patients were instructed to wear elastic stockings, but compliance was not formally assessed.

Digital photoplethysmography assessment

PPG assessments (ELCAT systems, Wolfrathausen, Germany) were performed as described previously.[6] A digital probe was attached to the medial calf on the affected side and a series of 8 active ankle dorsiflexions were performed as per manufacturer's instructions. Assessments were repeated 3 times, with and without a below-knee tourniquet inflated to 80 mmHg. All assessments were performed by trained personnel and the mean of the 3 measurements was used in each case.

Statistical analysis

All analyses were performed using SPSS computer software v11.5 (Statistical Package for Social Sciences, Mass, USA) and p values <0.05 were deemed significant. VRTs were grouped into times >20 s, 11−20 s and <11 s, reflecting legs with least, intermediate and most venous dysfunction, respectively. Healing and recurrence rates were calculated for each of these groups using Kaplan-Meier life tables[10] and groups were compared using the Log-rank test. Patients were analysed based on actual treatment received and not on intention to treat.

Results

A total of 500 patients were recruited to the ESCHAR study. PPG assessments were not achieved in 117, mainly due to joint stiffness and an inability to perform the necessary ankle movements ($n = 101$), but also due to machine failure ($n = 16$). In patients where PPG measurements were not achieved, 24 week ulcer healing was 51% compared to 74% where PPG assessments were obtained ($p < 0.001$, Log rank test). Ulcer recurrence in the group without PPG assessment was 28.3% at 1 year compared to 21.6% in legs where PPG was achieved ($p = 0.795$, Log rank test).

Of the 383 patients included in this study, 237 were treated with compression alone and 146 with compression plus surgery. This included 45 patients randomised to surgery who declined operation and one patient randomised to compression who insisted on surgery.

Incidence of deep venous reflux

All legs in the study had superficial venous reflux. Co-existent deep venous reflux was present in 196/500 patients (39%). The incidence of deep reflux was greater in legs with VRTs <11 s compared to the group with VRTs >20 s (46/107 vs 55/166 respectively, $p = 0.026$, Chi-squared test) (Table 1).

Table 1. Incidence of deep reflux within study population

a. Patients where VRT measurement was not achieved ($n = 117$)

	Deep reflux	
	Not present	Present
	66	51 (44%)

b. Patients with VRT measurement ($n = 383$)

		Compression alone ($n = 237$)		Compression plus surgery ($n = 146$)	
		Deep reflux		Deep reflux	
		Not present	Present	Not present	Present
VRTs with below-knee tourniquet	>20 s	70	32 (31%)	41	23 (36%)
	11−20 s	48	25 (34%)	28	19 (40%)
	<11 s	30	32 (52%)	21	14 (40%)

Legs treated with compression alone

a. VRT without below-knee tourniquet

For VRT assessments performed without tourniquet, there was no correlation between VRTs and healing or recurrence rates ($p = 0.258$, 0.196 respectively, Log rank test).

b. VRT with below-knee tourniquet

Using a tourniquet, the healing rates for the group with best VRTs (>20 s) were significantly greater than the patients with intermediate VRTs (11−20 s) which in turn were better than the group with poor VRTs (<11 s) (24 week healing rates 92%, 73% and 62% respectively, $p < 0.001$, Log rank test) (Fig. 1a). There was no correlation with recurrence ($p = 0.394$) (Fig. 1a).

Compression plus surgery

a. VRT without below-knee tourniquet

No correlation between VRT without tourniquet and healing or recurrence rates was seen ($p = 0.40$, 0.79 for healing and recurrence respectively, Log rank test).

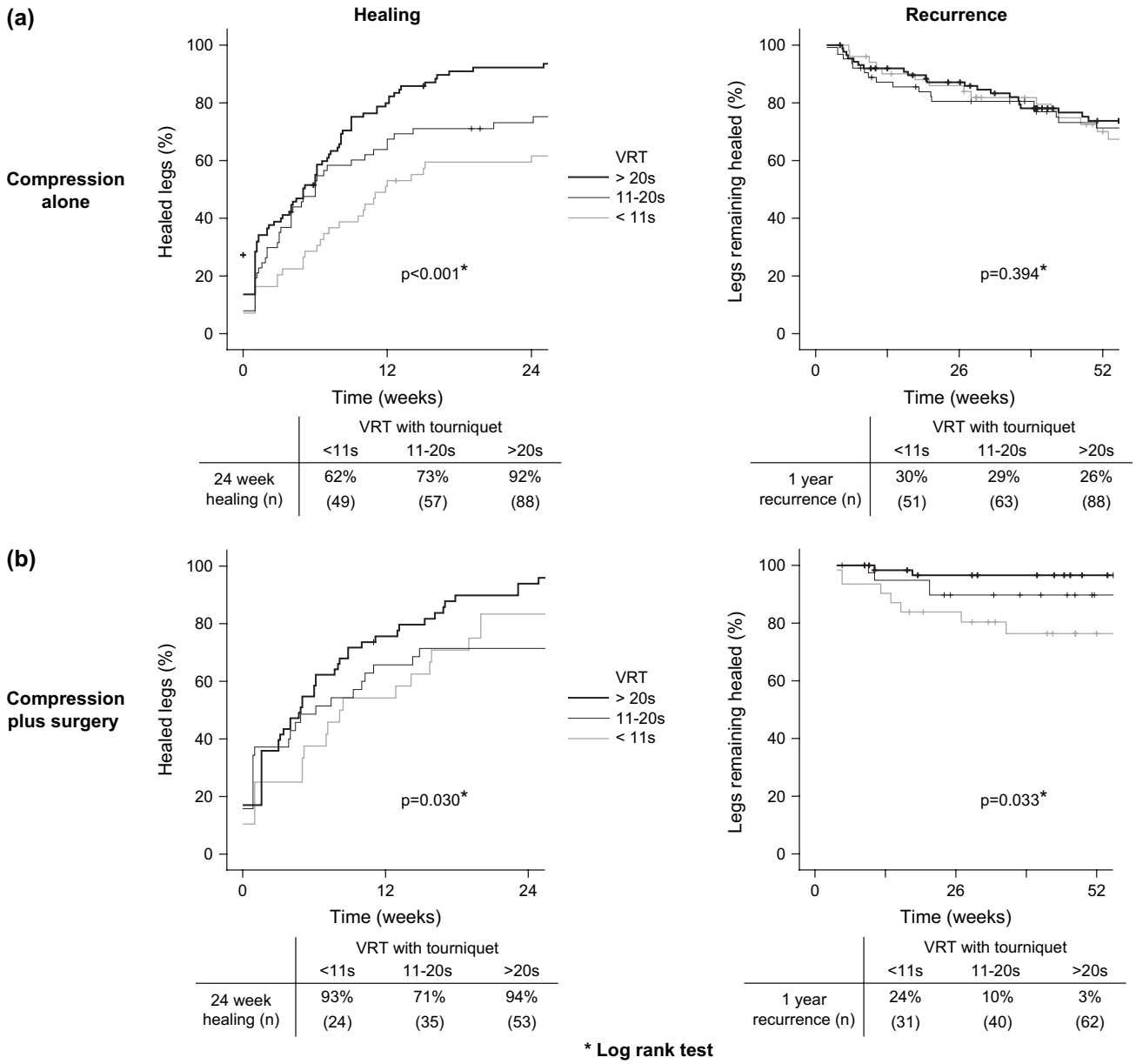

Fig. 1. Kaplan-Meier curves for healing and recurrence rates grouped by VRT with tourniquet for legs treated with compression (a) and compression plus surgery (b).

b. VRT with below-knee tourniquet

VRT measured with below-knee tourniquet correlated with ulcer healing for longer VRTs, but not for legs with VRTs < 11 s (Fig. 1b). However, there was a significant correlation between VRT with tourniquet and 1 year ulcer recurrence rates after surgery which were 24%, 10% and 3% for VRTs <11 s, 11−20 s and >20 s respectively ($p = 0.033$, Log rank test) (Fig. 1b).

Discussion

These data demonstrate that haemodynamic assessment using PPG is of value in predicting venous ulcer healing and recurrence, but only if a below-knee tourniquet is used. In patients where PPG assessment was not possible, ulcer healing rates were significantly lower than legs with successful VRT measurements. This may be due the higher incidence of ankle stiffness in this group.[11,12] The correlation was strongest for healing rates in legs treated with compression and recurrence rates in the group treated with compression and superficial venous surgery. Ulcer healing for legs in the surgery group showed a trend towards greater healing with increased VRT, although the small subgroup with VRT <11 s had an unexpected high healing rate.

This study supports the hypothesis that VRT reflects the severity of physiological venous dysfunction; although the correlation with clinical outcomes was only present using a tourniquet. A possible explanation is that the below-knee tourniquet compresses refluxing superficial veins and therefore mimics treatments such as saphenous surgery and compression bandaging. In this way, the tourniquet may effectively 'correct' for treatment. VRT with tourniquet may therefore reflect residual venous dysfunction or calf muscle pump failure and should logically correlate better with eventual clinical outcome for legs treated with compression or surgery. The correlation with ulcer recurrence was only present for legs treated with surgery, possibly because the tourniquet imitates surgery more than compression.

As PPG is a quick and non-invasive investigation, this correlation with venous ulcer healing and recurrence has many potential clinical advantages. Perhaps most importantly, patients could be informed and counselled of their likely outcome. Indeed, a predictive scoring system for ulcer healing incorporating PPG assessment has been created using these data.[13] Those predicted to have low healing or high recurrence rates may be targeted for further research or alternative treatment strategies such as skin grafting,[14] VAC therapy[15,16] or biological agents[17–19] although many of these remain unproven.

The use of superficial venous surgery reduces venous ulcer recurrence in some patients, particularly those without reflux in deep veins.[9,20] In an elderly population, it is important to avoid surgery in those unlikely to gain any clinical benefit. The measurement of VRT using a tourniquet has previously been shown to predict haemodynamic improvement after saphenous surgery[6] and inspection of Fig. 1b demonstrates that this correlation also exists for ulcer recurrence. Poor VRTs with below-knee tourniquet should logically be explained by the presence of deep venous reflux. Indeed, in this study population, the incidence of deep reflux was greater in legs with short VRTs. However, it should be noted that even in the group with normal VRT >20 s, deep reflux was present in 33% of cases, suggesting that the presence of anatomical deep venous reflux may not necessarily be associated with physiological dysfunction. The additional information provided by PPG could be used in combination with colour venous duplex to accurately identify those most likely to benefit from surgery, although further work is needed to refine this assessment pathway.

The use of colour venous duplex has revolutionised the investigation of venous disease while assessment of venous refill time has largely been limited to research activity. However, by assessing physiological dysfunction, this simple, well tolerated test correlates with clinical outcomes and could become an important adjunct to colour duplex in the investigation of patients with venous disease.

Acknowledgements

The authors would like to thank C Wakely, J Minor, K Harvey and A Sassano (Vascular Scientists) for performing PPG and venous duplex assessments; M Taylor, C Davies, G Woolfrey, G Turton, R Elley and J Waldron (Gloucestershire Leg Ulcer Service) for the assistance in the assessment and follow-up of patients and Mr C Foy (Medical Statistician). The ESCHAR study was funded by The NHS Executive South and West Research and Development Directorate, Southmead Hospital Research Foundation and the Medical Research Council.

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Accepted 26 November 2006
Available online 31 January 2007